

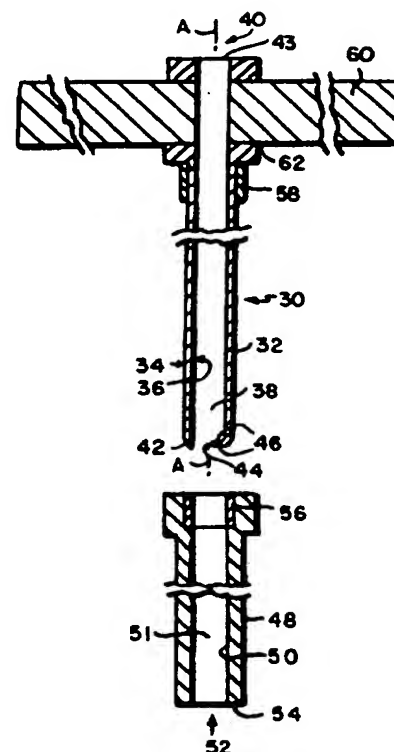


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61B 17/16, 17/32, A61F 2/46	A1	(11) International Publication Number: WO 96/27333 (43) International Publication Date: 12 September 1996 (12.09.96)
(21) International Application Number: PCT/US96/01923 (22) International Filing Date: 8 February 1996 (08.02.96) (30) Priority Data: 08/399,428 7 March 1995 (07.03.95) US (71) Applicant: INNOVASIVE DEVICES, INC. [US/US]; 734 Forest Street, Marlborough, MA 01752-3032 (US). (72) Inventors: HART, Rickey, D.; 11 Hillside Road, Plainville, MA 02762 (US). BARBER, F., Alan; 9 Post-N-Paddock, Frisco, TX 75034 (US). CHOW, James, C.; 3001 Caroline Drive, Mount Vernon, IL 63864 (US). (74) Agent: JIMENEZ, Mary, Raynor, Choate, Hall & Stewart, 53 State Street, Exchange Place, Boston, MA 02109 (US).		(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: APPARATUS AND METHODS FOR ARTICULAR CARTILAGE DEFECT REPAIR**(57) Abstract**

A bone plug removal tool (30) is described. The tool (30) includes a cylindrical cutting element (32) having an external surface (34) and having an internal surface (36) defining an internal bore (38) extending along a longitudinal axis (40) of the cutting element (32) from a proximal end (42) to a distal end (43). A cutting tooth (44) is located at the proximal end (42) of the cutting element (32) and extends into the internal bore (38). A replaceable outer cylindrical sheath (48) is arranged concentrically around the external surface (34) of the cylindrical cutting element (32). A bone plug emplacement tool (80) to be used in conjunction with the removal tool (30) is also disclosed. The emplacement tool (80) includes a cylindrical element (82) having an internal surface (84) defining an internal bore (86) extending along a longitudinal axis (87) of the element (82) from a proximal end (88). The internal surface (84) further defines an internal step (90) adjacent a distal end (92) of the element (82). A stem is disposed for coaxial movement within the element (82), the stem (94) having a proximal end disposed within the internal bore (86). A shoulder (98) is defined in the stem (94) for mating engagement within the internal distal step (90) of the element (82) in order to limit distal movement of the stem (94) within the internal bore (86). A kit incorporating the various tools is disclosed. The kit, for repair of an articular cartilage (112), includes the bone plug removal tool (30) of the invention, an elongated plunger (70) for insertion into the proximal end (42) of the cutting element (32) and for coaxial movement within it, the plunger (70) for displacing a bone plug (78, 118) from the distal end (43) of cutting element (32) and the bone plug emplacement tool (80) of the invention. Kits may also include a drill bit containing a depth stop. A method of repairing a defective articular cartilage is also described.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LJ	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

APPARATUS AND METHODS FOR ARTICULAR CARTILAGE DEFECT REPAIR

Field of the Invention

5 This invention relates to articular cartilage defects and their repair and more particularly to an apparatus and a method for effecting such repair.

Background of the Invention

Defects in articular cartilage associated with trauma and osteochondritis
10 dissecans represent a difficult challenge for surgeons. The patient can expect to face progressive deterioration over time leading to advanced osteochondritis, arthritis and the possibility of joint replacement. The knee as a weight-bearing joint is particularly susceptible to this problem, although similar injuries to the articular cartilage of other joints in humans and other
15 mammals also occur with regularity.

Fig. 1 illustrates a knee joint 10 between the distal end 11 (i.e., that surface farthest from the center of the body) of a femur 12 and the proximal end 13 (i.e., that surface closest to the center of the body) of the tibia 14. Portions 15, 17 of the connective tissue which movably ties the femur 12 to
20 the underlying tibia 14 and fibula 18 are shown. Normally interposed between opposing surfaces of the femur 12 and tibia 14 are lateral and medial meniscus cartilages, 21 and 23, respectively. The condyles 22 at the distal end 11 of the femur 12 are normally supported by the meniscus cartilages 21 and 23 on the proximal end 13 of the tibia 14. Normally, the distal end 11 of
25 femur 12, including the condyles 22 is covered by a layer 28 of cartilaginous material about 5 mm thick, referred to as the articular cartilage. Articular cartilage 28 forms a generally resilient pad which is fixed on the distal surface 11 of the femur 12 to protect the femur from wear and mechanical shock. The articular cartilage 28, when lubricated by fluid in the knee joint 10,
30 provides a surface which is readily slidable on the underlying surfaces of the meniscus cartilages 21 and 23 or on the proximal surface 13 of the tibia 14 if one or both of the meniscus cartilages 21, 23 should be partially or totally

-2-

absent. Nevertheless, the articular cartilage 28 may become damaged in that it may be torn 24 or holed or become excessively worn.

Methods have been used to repair such articular cartilage damage before it can spread or result in eventual injury or wear to the underlying condyles 22, meniscus cartilages 21, 23, or tissues associated with the tibia 12. It has been known to replace damaged articular cartilage with a layer of fibrous material. See U.S. Patent No. 5,067,964. Repairing defects in articular cartilage in human or other mammalian joints therefore requires materials that have been approved by the FDA for use in the human body. Is often problematic to find such materials that are commercially available and relatively low in cost in which completion of the repairs are within the skills of qualified orthopedic surgeons. Another repair method involves packing an articular cartilage defect with bits of cancellous and cortical bone (Soviet Patent SU 1454423, June 27, 1986) that have been chipped from defect-free bone. This latter technique avoids using foreign materials but, like the former methods, does not preserve the original orientation of bone and cartilage.

Prostheses have also been used for replacement of the joint itself. Problems encountered after implanting such prostheses are usually caused by the cements used to attach the prostheses to the host bone. Further, some prostheses associated with joint replacements are actually much larger than the degenerated tissue that needs to be replaced so that extensive portions of healthy bone are typically removed to accommodate the prostheses.

The need remains to develop apparatus and methods which are suitable for articular cartilage repair and which avoid problems associated with prior art methods, such as those discussed above.

Summary Of The Invention

The present invention is an apparatus for repairing articular cartilage defects, and methods of using the apparatus, that harvest and utilize intact

-3-

bone and intact articular cartilage plugs that preserve the natural orientation of the bone and articular cartilage.

One embodiment of the invention is a bone plug removal tool that includes a cylindrical cutting element having an external surface and having
5 an internal surface defining an internal bore extending along a longitudinal axis of the cutting element from a proximal cutting edge. A cutting tooth is engaged with the internal surface at the proximal cutting edge and extends into the internal bore. The tooth is substantially orthogonal to the longitudinal axis of the cutting element and is defined between orthogonally extending
10 surfaces disposed in parallel. A replaceable outer cylindrical sheath is arranged concentrically around the external surface of the cylindrical cutting element. The sheath also has an internal surface defining an internal bore extending along a longitudinal axis of the sheath. The sheath has a proximal terminus that is spaced-apart from the proximal cutting edge of the cylindrical
15 cutting element and the terminus is designed to engage a surface of the bone to define a depth stop for the cutting edge. In preferred embodiments, the cutting tooth is a single tooth and screw threads are disposed on the external surface of the cylindrical cutting element for mating with corresponding screw threads on the internal surface of the cylindrical sheath. A handle may be
20 engaged with a distal end of the tool for turning the tool into the bone once it has been driven to the desired depth. Thus, one aspect of the invention is a bone plug remover having an elongated body including two concentric elements in which an inner element is a cutting element and an outer element is replaceable and defines a depth stop for cutting.

25 Another embodiment of the invention is a bone plug emplacement tool to be used in conjunction with the bone plug removal tool. The preferred emplacement tool includes a cylindrical element having an internal surface defining an internal bore extending along a longitudinal axis of the element from a proximal end. The internal surface further defines an internal step
30 adjacent a distal end of the element. A stem is disposed for co-axial

-4-

movement within the element, the stem having a proximal end disposed within the internal bore. A shoulder is defined in the stem for mating engagement with the internal distal step of the element in order to limit distal movement of the stem within the internal bore. The proximal end of the stem, at the
5 limit of distal movement, is spaced-apart from the proximal end of the coaxial element, the respective proximal ends defining between them an internal bone plug receiving space for receiving a bone plug of a certain length. The stem may be moved from a distal position, where the shoulder and step are engaged and the respective proximal ends define the space for receiving a
10 bone plug, to a proximal position, where the stem is moved proximally within the internal bore and the bone plug is driven from the internal bone plug receiving space. A second step may be defined in the stem for limiting proximal movement. This second step is located distal to the first step and external to the cylindrical element. It is preferred that, in the distal position,
15 the second step and the distal end of the element are at a distance from each other that is equal to, or less than, the length of the bone plug.

A further embodiment is a kit incorporating the various tools. The kit for repair of an articular cartilage includes the bone plug removal tool of the invention, an elongated plunger for insertion into the proximal end of the
20 cutting element and for coaxial movement within it, the plunger for displacing a bone plug from the distal end of the cutting element and the bone plug emplacement tool of the invention. Kits may also include a drill bit containing a depth stop for removing a portion of damaged articular cartilage.

A further embodiment of the invention also includes the combination of
25 the bone plug emplacement tool of the invention and an excised bone plug contained within the internal bone plug receiving space of the emplacement tool.

The invention also pertains to a method of repairing a defective articular cartilage. The method includes the steps of removing a section of
30 defective articular cartilage from a site of cartilage damage and forming a

-5-

hole of sufficient depth to penetrate bone underlying the site of defective articular cartilage. Next, a bone plug comprising intact bone and intact articular cartilage adhering thereto is removed from a bone lacking defective articular cartilage and is placed into the hole at the site of articular cartilage damage, so that the intact articular cartilage of the bone plug is co-extensive, and in lateral registration (i.e., aligned) with, articular cartilage external to the bone hole at the site of cartilage damage. The term "intact" in this context means that the bone and overlying articular cartilage undergo minimal physical disturbance during the removal process.

10

Brief Description Of The Drawings

Other objects and purposes of the invention will be apparent to persons knowledgeable in this art upon reading the following description and inspecting the accompanying drawings which show:

15 Fig. 1 is a fragmentary front elevation view of a human knee joint with sufficient tissue removed to show the articular cartilage on the condyles of the femur, and further showing a damaged area in the articular cartilage.

Fig. 2 is an exploded cross sectional view of a bone plug removal tool of the present invention.

20 Fig. 3 is the bone plug removal tool of Fig. 2 with the cylindrical sheath and cylindrical cutting element joined.

Fig. 4A is a proximal end view of the bone plug removal tool of the present invention illustrating one embodiment of the cutting tooth.

25 Fig. 4B is a proximal end view of the bone plug removal tool of the present invention illustrating another embodiment of the cutting tooth.

Fig. 5 is a side elevation view of a plunger of the present invention that is designed to remove a bone plug from within the bone plug removal tool.

30 Fig. 6 is a cross sectional view of a bone plug emplacement tool in its distal position.

-6-

Fig. 7 is a cross sectional view of the bone plug emplacement tool of Fig. 6 in its proximal position.

Figs. 8A through 8D are cross-sectional views of a fragment of bone through section 8-8 of Fig. 1 illustrating the orientation of the bone hole and bone plug of the present surgical technique.

Fig. 8A is a cross section through a bone that contains a defect in the articular cartilage.

Fig. 8B is a cross section through a bone whose defective cartilage area has been removed and into which a bone hole has been drilled. A bone plug is illustrated in proper orientation for insertion.

Fig. 8C illustrates a bone plug received within a drilled bone hole.

Fig. 8D illustrates a plurality of drilled bone holes within an articular cartilage defect.

Fig. 9 is a front elevation view of a plurality of bone plugs received within a single drilled bone hole within an articular cartilage defect.

Detailed Description Of The Invention

Reference is now made to Figs. 2-3 which illustrate one embodiment of the present bone plug removal tool. The bone plug removal tool 30 is a substantially cylindrical device made out of two pieces of surgical stainless steel. The tool 30 is formed into a cylindrical cutting element 32 and a cylindrical sheath 48 that is arranged concentrically around the cylindrical cutting element 32. Cutting element 32 has an external surface 34 and an internal surface 36. The internal surface 36 further defines an internal bore 38 extending along a longitudinal axis 40 (arrows A-A) of the cylindrical cutting element 32. The bore 38 extends distally away from a proximal cutting edge 42. In the present context, the term "proximal" refers to those portions of the apparatus that are closest to the center of the body or, alternately, are furthest away from the operator of the apparatus. The term "distal" refers to those portions of the apparatus that are furthest from the

-7-

center of the body or, alternately, are closest to the operator of the apparatus. The internal bore 38 extends from the proximal cutting edge 42 to the distal end 43 of the cylindrical cutting element 32 from which a bone plug can be removed by the operator after bone plug extraction has been completed.

5 The proximal cutting edge 42 is sharpened so that any bone entering the internal bore 38 is cut from the surrounding bone. An excised bone plug trapped within bore 38 can move freely into this space and out the distal end 43 after the plug excision procedure has been completed, as discussed in more detail below.

10 At least one cutting tooth 44 is engaged with the internal surface 36 of the cylindrical cutting element 32 at the proximal cutting edge 42. This tooth 44 extends into the internal bore 38 in a direction that is substantially orthogonal to longitudinal axis 40 of the cylindrical cutting element 32. The cutting tooth 44 is defined by orthogonally extending tooth surfaces 46 that
15 are disposed in parallel. Although a plurality of such teeth may be orthogonally disposed at the proximal cutting edge 42, in the most preferred embodiments of the present invention, only a single cutting tooth is necessary. As shown in Fig. 4A, the cutting tooth 44 is preferably rectangular or square in shape. It is also understood, however, the cutting tooth 44 may be
20 generally triangular in shape as shown in Fig. 4B. The cutting tooth 44, moreover, preferably extends one-fifth of the diameter of the bore 38, although it may range from approximately 1/16 to 1/4 of the bore 38. When the bone plug removal tool 30 is rotated after insertion (to be described in more detail below), the core bone is forced to break loose from the
25 surrounding bone at the cutting edge 42 and the cutting tooth 44 is embedded into the bone. When the tool 30 is extracted, the bone plug is extracted with it. The cutting tooth 44 will also cut a groove along the length of the bone plug which provides additional bone strength when the bone plug is emplaced into a bone hole, as discussed more fully below.

-8-

Referring again to Figs. 2 and 3, the outer cylindrical sheath 48 is arranged concentrically around the external surface 34 of the cylindrical cutting element 32. The sheath has an internal surface 50 that also defines an internal bore 51 extending along longitudinal axis 52 of the sheath 48. In the embodiment illustrated, the outer cylindrical sheath 48 is removably engaged with the cylindrical cutting element 32 by way of matching screw threads 56, 58 located on the internal surface 50 of the cylindrical sheath 48 and on the external surface 34 of cylindrical cutting element 32, respectively. Therefore, the outer cylindrical sheath 48 is removable and may be replaced by another outer sheath having different dimensions by mating the corresponding screw threads. It is particularly preferred that outer cylindrical sheath 48, when engaged with the cylindrical cutting element 32, have a proximal terminus 54 that is not co-extensive with the proximal cutting edge 42 of the cutting element 32. Specifically, the proximal terminus 54 of outer cylindrical sheath 48 is spaced apart from the proximal cutting edge 42 by a distance that defines a depth stop distance X. The depth stop distance X defines the length of the bone plug that is to be removed.

As shown in Fig. 2, an elongated, preferably cylindrical handle 60 may cooperate with the adjacent distal end 43 of the cutting element 32 by way of a second bore 62 that extends through the cutting element 32 orthogonally to the longitudinal axis 40 of the cylindrical cutting element 32. Handle 60 may be inserted after the tool has been driven to the desired depth and is used for rotating the tool to cause the bone to break at proximal cutting edge 42.

It will be appreciated that various other embodiments are intended to be encompassed by the present bone plug tool. For example, handle 60 may be replaced by a conventional screw head (not shown) having a slot defined in it for receiving a screw driver or other, similar device. Handle 60 may also be replaced by a conventional hexagonal nut (not shown) which designed to receive a conventional socket wrench, socket driver or attached drill head.

Moreover, although the cutting element 32 is preferably driven into the bone

-9-

without any rotational movement, such as by hammering or tapping, it is also understood that the cutting element 32 may be screwed or twisted into the bone by means of a screwdriver, socket wrench or other similar device (not shown). In addition, corresponding threads 56, 58 may be replaced in other
5 embodiments by conventional spring loaded snap-fit linkages (not shown). The exact nature of the handle and the nature of the removable coupling between the cylindrical cutting element and the outer cylindrical sheath is not intended to limit the scope of the invention in any way.

The dimensions of the plug removal tool 30 may vary according to the
10 surgical procedures. In preferred embodiments, however, the bone plug removal tool 30 is about 6 inches (152.4 mm) in overall length. If a handle is used, the handle 60 is about 4 inches (101.6 mm) in total length with a diameter of about .31 inches (7.9 mm). The outer cylindrical sheath 48 has an outside diameter of 0.30 inch (7.6 mm) to provide sufficient surface area
15 to effectively limit the depth of penetration of the internal cylindrical cutting element 32. The distance between the respective proximal ends of the cylindrical sheath 48 and the cylindrical cutting element 32 will of necessity vary according to the depth of the bone plug. It is contemplated that this distance will vary between 5 mm and 15 mm.

20 The outside diameter of the cylindrical cutting element 32 at the proximal cutting edge 42 may also vary but is most preferably about 0.25 inches (6.3 mm) with a bore of about 0.196 inches (4.9 mm) inside diameter. Although the bore will preferably range between 4.5 mm and 10 mm, it will again be appreciated that this inside diameter can be smaller or larger
25 depending upon the circumstances.

As discussed above, the bone plug can move freely through internal bore 38 and pass out from the distal end 43 of cutting element 32 after the plug removal procedure has been completed. Fig. 5 illustrates a plunger 70 that is designed to accomplish this. Plunger 70 includes a shaft 72 having a
30 proximal end 74 and a distal portion 76 whose outside diameter is

-10-

significantly larger than the outside diameter of the rest of the shaft. The differences in outside diameter between the shaft 72 and the distal portion 76 form a step 77 at the junction of the distal portion 76 and shaft 72. The outside diameter of the shaft is sufficiently small so that shaft 72 can be
5 passed between the cutting tooth 44 and the opposite, internal surface 36 of the cylindrical cutting element 32. An exemplary plunger that may be used with the bone plug removal tool has a shaft of about 0.125 inches (3.17 mm) in diameter and at length of about 7 inches (177.8 mm) between its proximal end 74 and the step 77.

10 Figs. 6 and 7 illustrate a bone plug emplacement tool 80 used to drive an excised bone plug into a drilled bone hole so that defective articular cartilage may be repaired. Fig. 6 also shows a bone plug 78 in place within the emplacement tool 80. Bone plug emplacement tool 80 includes cylindrical element 82 having an internal surface 84 defining an internal bore 86.

15 Element 82 has an expanded section 83 adjacent distal end 92. The internal bore 86 extends along a longitudinal axis 87 of the element 82 from a proximal end 88 of the element 82. Element 82 has a distal end 92. The internal surface 84 further defines, adjacent the distal end 92 of the element 82, an internal step 90.

20 A stem 94, which may be solid, is disposed within the internal bore 86 and is adapted for co-axial (i.e. distal-proximal) movement. Stem 94 does not have an uniform outside diameter but includes a first shoulder 98 that is designed to mate in facing relationship to the internal step 90 of the cylindrical element 82. When first shoulder 98 and internal step 90 are thus
25 engaged, distal movement of the stem within the internal bore is halted. In this position (Fig. 6), the proximal end 96 of stem 94 is located within internal bore 86 and is spaced apart from the proximal end 88 of the cylindrical element 80. The respective proximal ends 88, 96, define between them an internal bone plug receiving space that is configured to receive the

-11-

bone plug 78 that is to be emplaced. In the embodiment illustrated, the stem 94 extends distally from the distal end 92 of cylindrical element 82.

At some distance from distal end 92, the stem 94 has defined in it a second shoulder 100. The second shoulder 100 is designed to engage with the distal end 92 of element 82 and this engagement limits the proximal movement of the stem 94 within the internal bore 86. The distance (Z) between the second shoulder 100 and distal end 92 of the cylindrical element 82 is designed to be at least equal to the longest dimension of the bone plug 78. Similarly, the distance (Z') between the proximal end 96 of stem 94 and the proximal end 88 of the cylindrical element 82 is also at least equal to the longest dimension of the bone plug 78 and equal in length to the length of the internal bone plug receiving space. Proximal movement of the stem 94 within the internal bore 86 of the emplacement tool 80 will completely disgorge the bone plug 78 into a drilled bone hole. In preferred embodiments, the distance (Z) between the second shoulder 100 and the distal end 92 of the cylindrical element 82 is slightly less than the bone plug depth. For instance, in a 5 mm long bone plug, Z is 4 mm; for a 10 mm long bone plug, distance Z is 9 mm; for a 15 mm bone plug, distance Z is 14 mm, and so on. Thus, the distance (Z') between the proximal end 96 of the stem 94 and the proximal end 88 of the cylindrical element 82 is also slightly less than the bone plug depth. Specifically, if the bone plug is 5 millimeters long, the distance (Z') between the respective proximal ends 88, 96 is 4 millimeters so that one millimeter of bone will protrude from the proximal end 88 of the cylindrical element 82. This protruding section assists the operator in finding the drilled bone hole prior to emplacement.

The stem 94 is adapted for movement from a distal position (Fig. 6), where the first shoulder 98 and the internal step 90 are engaged and the respective proximal ends 88, 96 define between them the internal bone plug receiving space. The stem 94 then moves to a proximal position (Fig. 7) where the second shoulder 100 engages with the distal end 92 of cylindrical

-12-

element 82 and the bone plug is disgorged from within the internal bone plug receiving space, as described below. An exemplary emplacement tool that is compatible with the bone plug removal tool discussed previously has a cylindrical element that defines an internal bore of about 0.196 inches (4.9 mm) inside diameter. The outside diameter of the cylindrical element may be about 0.25 inches (6.3 mm) in diameter. The length of the cylindrical element from its proximal end to the beginning of the expanded section 83 may be about 5.5 inches (139.7 mm) in length.

The surgical technique described herein is preferably performed arthroscopically using conventional equipment, although open techniques may be utilized should proper bone plug insertion prove impossible by arthroscopic means. Before surgery, a bone plug removal tool of the present invention is prepared. A standard anterolateral or medial or superior portal is used to introduce a 4.5 mm, 30° oblique arthroscope, and a shaver is applied through an anteromedial portal to prepare the articular cartilage defect. After shaving the degenerated cartilage in the vicinity of the defect, an 8 mm skin incision is made on the superolateral corner of the patellofemoral joint. The bone plug removal tool 30 is inserted through this portal and at least one cylindrical bone plug (5 mm in diameter and 10 mm in length) is taken from the lateral wall of the patellar groove, located outside the patellofemoral joint. A bone plug may also be taken from the anterolateral side of the intercondylar area. Three holes, each with a diameter of 4.8 mm, are then made using a drill bit through the anteromedial portal. The bone plug is removed from the removal tool 30 using the plunger 70 and positioned within the emplacement tool 80, as described below. The bone plug emplacement tool 80 of the invention containing the bone plug in its correct orientation is placed over the hole through this portal and the bone plug is pushed into the hole using the emplacement tool 80, as described herein.

Referring generally to Figs. 8A-8D, the present invention contemplates repairing a defect or damaged area 110 in an articular cartilage 112 by

-13-

removing a conveniently shaped (for example circular) portion 114 of the defective articular cartilage layer 112 and a portion 115 of the underlying bone 116. Fig. 8A illustrates the general principle, discussed more fully below, that the surface area of the bone portion removed 115 is not necessarily co-extensive with the surface area 114 of cartilage removed. The edges 122 of the defect 110 are debrided to create vertical walls and sharp edges. The base of the defect is shaved smooth but is not abraded through to the subchondral bone. The size of the removed portion 114 is kept to a minimum but is large enough to include the whole of the damaged cartilage area.

The bone is drilled with a hand or power drill containing a drill bit that most preferably has an expanded outside diameter (i.e., a depth stop countersink) located some distance distal to the proximal end of the drill bit. An exemplary drill bit used with the present methodology has a cutting surface exactly equal to the chosen length of the bone plug. That is, the cutting surface can be between about 5 mm and 15 mm in length. The outside diameter of such an exemplary drill bit is very slightly undersized relative to the inside bore diameter of the bone core removal tool. In particular, an internal bore of 0.196 (4.97 mm) inside diameter for the cylindrical cutting element of a bone core removal tool would require a drill bit of 0.190 (4.82 mm) inches outside diameter. The difference of 0.006 (0.15 mm) inches is necessary for the required interference fit of the bone plug within the drilled bone hole. The outside diameter of the drill bit begins its expanded depth stop section at a distance above the proximal end that is equal to the depth of the bone plug. This expanded section may be 0.25 inches (6.35 mm) in diameter and can be about 6 inches (152.4 mm) long.

Bone holes drilled into the underlying bone may be of any depth but are most preferably about 5 mm to about 15 mm in depth. It is most preferred that excised plugs of articular cartilage with the underlying subchondral cancellous bone attached have a total length of about 10 mm. This will

-14-

provide individual bone plugs having about 5 mm of cartilage and 5 mm of bone or other similar combinations such as 2mm of cartilage and 8 mm of bone, 3 mm of cartilage and 7 mm of bone, etc.

Depending on the size of the defect and of the underlying bone hole, several bone holes may be drilled, each bone hole designed to receive a single bone plug (Fig. 8D) or a single bone hole may be drilled to receive a plurality of bone plugs (Fig. 9).

Following removal of the articular cartilage portion of the damaged area 110, as well as the underlying bone, a correspondingly sized and shaped bone plug 118 is inserted, first into and through the opening 114 left in the articular cartilage layer 112, and then into the underlying drilled bone hole 120. The bone plug 118 contains both bone 116A and its overlying articular cartilage 112A. These plugs will most preferably be taken from the non weight-bearing surfaces of the joint principally in the intracondylar notch and the periphery of the condyle. The bone plug 118 is inserted into the drilled bone hole 120 so that the articular cartilage layer 112A of bone plug 118 is in lateral registration with (i.e., is aligned with) the articular cartilage layer 112 surrounding the drilled bone hole 120.

The bone plug 118 is of sufficient shape to maintain a frictional fit within the drilled bone hole 120 and will remain there until such time as tissue ingrowth from the surface of the bone and peripheral, cut edges 122 of the articular cartilage layer 112 surrounding the bone hole 120 more permanently fix the bone plug 118 in place.

Bone plugs 118 may be positioned within a single bone hole 120 so that their respective outer peripheral edges are not in contact with each other. More preferably, individual bone plugs 118 located in their respective bone holes 120 may have their centers between 3 mm and 5 mm apart (See Fig. 8D). The peripheral edges 113, 115 of a given bone plug 118 are preferably positioned at some distance (Y) from the cut edges 122 of the defect and it is preferred that this distance be no further than about 5 mm.

-15-

These rules for bone plug spacing and orientation allow for a variety of possible configurations. For example, an articular cartilage defect 10 mm in diameter may accommodate one 5 mm diameter plug in the center of the defect. A defect 20 mm in diameter may be divided into four, 10 mm diameter quadrants and four holes drilled in the underlying bone. The defect therefore receives a total of four bone plugs.

Although the bone plug 118 is designed to have a friction fit into the drilled bone hole 120, several temporary fixation techniques are available. One such technique involves sewing sutures through the respective peripheral edges 113 of the articular cartilage layer 112A adhering to the bone plug and the articular cartilage 122 of the surrounding tissue. Alternatively, an adhesive layer (not shown) may be provided between the bone plug 118 and drilled bone hole 120. This adhesive layer allows time for sufficient ingrowth of tissue from the surrounding environment so that bone plug is locked into place in the bone hole. Various bio-adhesives are well known in the art. See for example U.S. Patent 5,067,964 (fibrinogen and thrombin sealant). Bone growth or cartilage growth promoting chemical factors may also be added. These may include cartilage-derived growth factor (CDGF- See U.S. Patent 5,376,636), various interleukins, colony-stimulating factor (CSF), osteopontin, platelet-derived growth factor (PDGF) and bone morphogenic protein (BMP-1). See also U.S. Patent 5,373,503, incorporated herein by reference.

In use, the bone plug removal tool 30 is positioned above the bone/cartilage surface and the proximal cutting edge 40 of the cylindrical cutting element is preferably tapped with a hammer (not shown) to seat the proximal cutting edge 40. When the tool 30 is fully seated in the bone, the handle 60 is turned a minimum of 360° degrees and the cylindrical cutting element 32 engages the bone down to a depth that is limited by contact of the proximal terminus of the outer sheath 54 with the bone surface. The outer sheath 54 does not cut into the bone. The tool 30 is then pulled distally away from the bone with a twisting action to remove the bone plug. The plunger

-16-

70 is then inserted through the proximal cutting edge 42 of the bone plug removal tool 30 to push or tap the bone plug through the internal bore 38 and out the distal end 43 of the bone plug removal tool 30. The excised bone plug is then manually inserted, typically by the surgeon, into the receiving space of the emplacement tool 80, articular cartilage surface 112A first. This insures proper orientation of the bone plug within the receiving space so that the excised articular cartilage layer 112A is engaged with the proximal end of the stem 96. It is particularly preferred that about one millimeter (1 mm) of underlying bone protrude from the proximal end 88 of the cylindrical element 82. This configuration allows the operator to find the drilled bone hole more easily. Once located, the bone plug is pressed into the drilled bone hole by moving the stem 94 from the distal to the proximal position so that the excised bone plug can be disgorged into the bone hole. The holes drilled in the donor defects are filled with collagen plugs.

Post operative rehabilitation may include nonweight bearing for eight weeks with crutches. Full active motion of the knee will be encouraged such as "nonweight bearing" exercise with a stationary bike using minimal resistance but high speed. This is useful for thigh rehabilitation as soon as pain and swelling permits. Running and pivoting activities should not be allowed until after healing is confirmed either radiographically or by relook arthroscopy.

An exemplary prospective study to assess the effectiveness of this technique is now described. Patients are selected with significant full thickness articular cartilage defects located on the weight bearing surface of the femur. To be included in the study, patients are a minimum age of 14 years, have a thickness defect in the distal femoral condyle that includes those caused by osteochondritis dissecans and trauma that is at least 10 mm but no larger than 30 mm in diameter, adequate bone density, a willingness to comply with the study protocol, and a commitment to return for at least two years follow up. No patient with an active infection, who does not meet all

-17-

of the inclusion criteria, or who has had prior knee surgery that would compromise the vascular supply is included.

Preoperative assessment includes a history including any identifiable etiology of the defect, a physical and radiographic evaluation, and the completion of both the Lysholm knee scoring scale and Tegner activity level scale. The objective evaluation includes tests for mensical signs, range of motion, atrophy, effusion, instability (Lachman, anterior drawer, and pivot shift), and patellofemoral problems. Baseline radiographs are obtained. The findings at surgery and procedures performed are recorded.

Post operative assessments occur at intervals of 1, 2, 3, 6, 12, and 24 months. These assessments are essentially the same as the preoperative evaluations and include the data for the Lysholm and Tegner scale and knee radiographs.

It should be understood that the preceding is merely a detailed description of certain preferred embodiments. It therefore should be apparent to those skilled in the art that various modifications and equivalents can be made without departing from the spirit or scope of the invention.

What is claimed is:

-18-

1. A bone plug removal tool, comprising:
a cylindrical cutting element having an external surface and having an internal surface defining an internal bore extending along a longitudinal axis of said cutting element from a proximal end to a distal end of said cutting
5 element;
a cutting edge located at the proximal end of said cutting element for cutting a plug of bone as the cutting element is driven into a bone;
at least one cutting tooth located at the proximal end of said cutting element and extending into said internal bore, said cutting tooth substantially
10 orthogonal to the longitudinal axis of the cutting element; and
an outer cylindrical sheath arranged concentrically around the external surface of the cylindrical cutting element, the sheath having an internal surface defining an internal bore extending along a longitudinal axis of said sheath, the sheath having a proximal terminus that is spaced-apart from the
15 cutting edge of the cylindrical cutting element.
2. The tool of claim 1, wherein the proximal terminus of the sheath is adapted to engage a surface of the bone and defines a depth stop for the cutting edge.
20
3. The tool of claim 1, wherein the plug of bone cut by the tool has a length equal to the distance between the proximal terminus of the cylindrical sheath and the proximal cutting edge of the cutting element.
- 25 4. The tool of claim 1, wherein the cutting tooth is a single tooth.
5. The tool of claim 1, wherein the cutting tooth is defined between two orthogonally extending surfaces disposed in parallel.

-19-

6. The tool of claim 1, wherein the cutting tooth has a substantially rectangular planar surface.
7. The tool of claim 1, wherein the cutting tooth has a substantially triangular planar surface.
8. The tool of claim 1, wherein the cutting tooth extends approximately one-fifth of the diameter of the internal bore.
9. The tool of claim 1, further comprising screw threads disposed on the external surface of the cylindrical cutting element for mating engagement with corresponding screw threads on the internal surface of the cylindrical sheath.
10. The tool of claim 1, further comprising a handle engaged with the distal end of the tool, the handle cooperating with the tool in a direction orthogonal to the longitudinal axis of the cutting element, for turning the tool into the bone.
11. The tool of claim 1, further comprising a slotted nut engaged with the distal end of the tool, the slotted nut for cooperation with a blade for turning the tool into the bone.
12. The tool of claim 1, further comprising a hexagonal nut for cooperation with a socket driver for turning the tool into the bone.
13. The tool of claim 12, wherein the hexagonal nut is capable of being attached to a drill.

-20-

14. A bone plug emplacement tool, comprising:

a cylindrical element having an internal surface defining an internal bore extending along a longitudinal axis of said element from a proximal end thereof, the internal surface further defining an internal step adjacent a distal end of the element;

a stem disposed for co-axial movement within the element, the stem having a proximal end disposed within the internal bore; and

a shoulder defined in the stem for mating engagement with the internal distal step of the element in order to limit distal movement of the stem within the internal bore, wherein the proximal end of the stem, at the limit of distal movement, is spaced-apart from the proximal end of the cylindrical element, the respective proximal ends of the stem and element define therebetween an internal bone plug receiving space for receiving a bone plug to be emplaced, wherein the stem is adapted for movement from a distal position, where the shoulder and step are engaged and the respective proximal ends of the stem and element define therebetween a space for receiving a bone plug, to a proximal position, where the stem is moved proximally within the internal bore and the bone plug is driven from the internal bone plug receiving space.

20

15. The tool of claim 14, further comprising a second shoulder defined in the stem for limiting proximal movement thereof, the second shoulder located distal to the first shoulder and external to the cylindrical element, wherein the second shoulder is for engagement with the distal end of the cylindrical element when the stem is in its proximal position.

25

16. The tool of claim 15, wherein in the distal position, the second shoulder and the distal end of the cylindrical element are at a distance from each other that is equal to, or less than, the length of the bone plug.

30

-21-

17. A kit for repair of articular cartilage, comprising:

(a) a bone plug removal tool, comprising:

5 a cylindrical cutting element having an external surface and having an internal surface defining an internal bore extending along a longitudinal axis of said cutting element from a proximal end to a distal end of said cutting element;

a cutting edge located at the proximal end of said cutting element for cutting a plug of bone as the cutting element is driven into a bone;

10 at least one cutting tooth located at the proximal end of said cutting element and extending into said internal bore, said cutting tooth substantially orthogonal to the longitudinal axis of the cutting element; and

an outer cylindrical sheath arranged concentrically around the external surface of the cylindrical cutting element, the sheath having an internal surface defining an internal bore extending along a longitudinal axis of said sheath, the sheath having a proximal terminus that is spaced-apart from the cutting edge of the cylindrical cutting element;

15 (b) an elongated plunger for insertion into the proximal end of the cutting element of the tool of claim (a) and for coaxial movement therewithin, the plunger for displacing a bone plug from the distal end of cutting element; and

(c) a bone plug emplacement tool, comprising:

25 a cylindrical element having an internal surface defining an internal bore extending along a longitudinal axis of said element from a proximal end thereof, the internal surface further defining an internal step adjacent a distal end of the element;

a stem disposed for co-axial movement within the element, the stem having a proximal end disposed within the internal bore; and

30 a shoulder defined in the stem for mating engagement with the internal distal step of the element in order to limit distal movement of the

-22-

- stem within the internal bore, wherein the proximal end of the stem, at the limit of distal movement, is spaced-apart from the proximal end of the cylindrical element, the respective proximal ends of the stem and element define therebetween an internal bone plug receiving space for receiving a
- 5 bone plug to be emplaced,
- wherein the stem is adapted for movement from a distal position, where the shoulder and step are engaged and the respective proximal ends of the stem and element define therebetween a space for receiving a bone plug, to a proximal position, where the stem is moved proximally within
- 10 the internal bore and the bone plug is driven from the internal bone plug receiving space.
18. The kit of claim 17, further comprising: (d) a drill bit containing a depth stop.
- 15
19. The kit of claim 17, wherein the proximal terminus of the sheath defined by the tool in (a) is adapted to engage a surface of the bone and defines a depth stop for the cutting edge.
- 20
20. The kit of claim 17, wherein the plug of bone cut by the tool defined in (a) has a length equal to the distance between the proximal terminus of the cylindrical sheath and the proximal cutting edge of the cutting element.
21. The kit of claim 17, wherein the cutting tooth defined by the tool in (a)
- 25 is a single tooth.
22. The kit of claim 17, wherein the cutting tooth defined by the tool in (a) is defined between two orthogonally extending surfaces disposed in parallel.

-23-

23. The kit of claim 17, wherein the cutting tooth defined by the tool in (a) has a substantially rectangular planar surface.
24. The kit of claim 17, wherein the cutting tooth defined by the tool in (a)
5 has a substantially triangular planar surface.
25. The kit of claim 17, wherein the cutting tooth defined by the tool in (a) extends approximately one-fifth of the diameter of the internal bore.
- 10 26. The kit of claim 17, wherein the tool defined in (c) further comprises a second shoulder defined in the stem for limiting proximal movement thereof, the second shoulder located distal to the first shoulder and external to the cylindrical element, wherein the second shoulder is for engagement with the distal end of the cylindrical element when the stem is in its proximal position.
- 15 27. The kit of claim 26, wherein the tool defined in (c) in the distal position, the second shoulder and the distal end of the cylindrical element are at a distance from each other that is equal to, or less than, the length of the bone plug.
- 20 28. In combination, the bone plug emplacement tool of claim 10 and an excised bone plug contained within the internal bone plug receiving space of the emplacement tool.
- 25 29. In a bone plug remover having an elongated body, wherein the improvement comprises a body including two concentric elements in which an inner element is a cutting element and an outer element is replaceable and defines a depth stop for cutting.

30

-24-

30. A method of repairing a defective articular cartilage, comprising:
removing a section of defective articular cartilage from a site of
cartilage damage;
forming a hole of sufficient depth to penetrate bone underlying said site
5 of defective articular cartilage;
removing a bone plug comprising intact bone and intact articular
cartilage adhering thereto from a bone lacking defective articular cartilage;
and
placing into the hole at the site of articular cartilage damage said bone
10 plug comprising intact bone and intact articular cartilage adhering thereto.
31. The method of claim 30, wherein the bone plug comprising intact bone
and intact articular cartilage adhering thereto is placed into the hole at the site
of articular cartilage damage so that the intact articular cartilage of the bone
15 plug is a co-extensive, and in lateral registration with, articular cartilage
external to the bone hole at the site of cartilage damage.
32. The method of claim 30, wherein the step of removing comprises:
contacting a proximal cutting edge of a cylindrical cutting element with
20 a surface of the bone, the cutting element having an internal surface defining
an internal bore extending along a longitudinal axis of said cutting element
from the proximal cutting edge, and an outer cylindrical sheath arranged
concentrically around the external surface of the cylindrical cutting element,
the sheath having a proximal terminus that is spaced-apart from the proximal
25 cutting edge of the cylindrical cutting element;
driving the cutting element into the bone surface so that the proximal
cutting edge is driven into the bone to form a bone plug containing bone and
adhering articular cartilage and the proximal terminus of the sheath rests
against the surface of the bone;

-25-

turning the cutting element at least 360° to separate the bone plug from the bone; and

removing the bone plug containing intact bone and intact adhering cartilage from the bone.

5

33. The method of claim 32, wherein the step of placing comprises:

inserting the bone plug, articular cartilage first, into an internal bone plug receiving space formed within a bone plug emplacement tool;

10 contacting the emplacement tool and received bone plug with the formed hole;

disgorging the bone plug and adhering articular cartilage into the formed hole so that the healthy, adhering articular cartilage of the bone plug is co-extensive, and in lateral registration with, articular cartilage external to the bone hole.

15

1/4

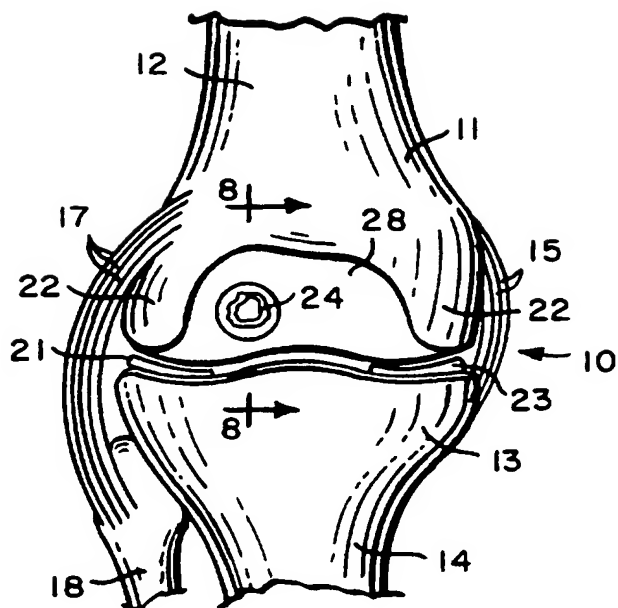


FIG. 1

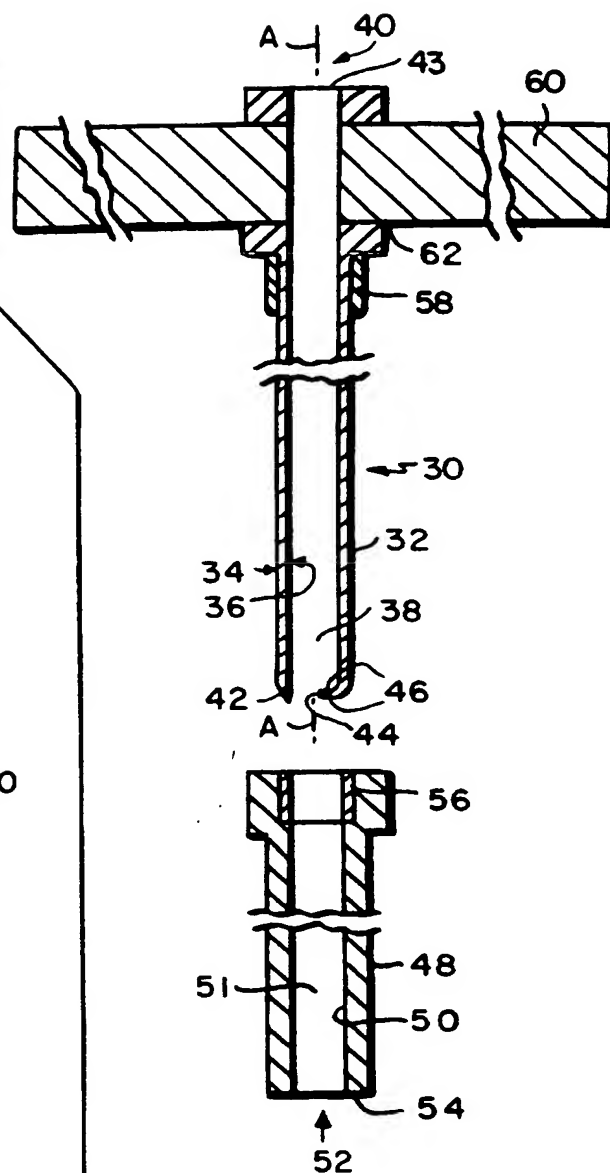
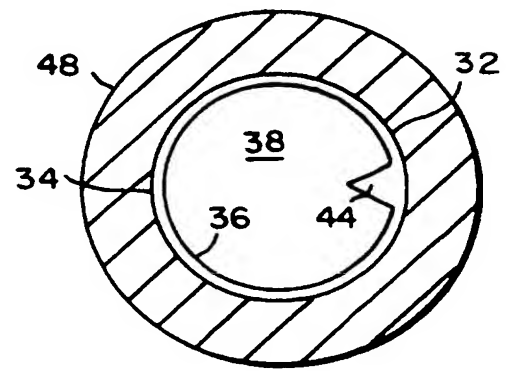
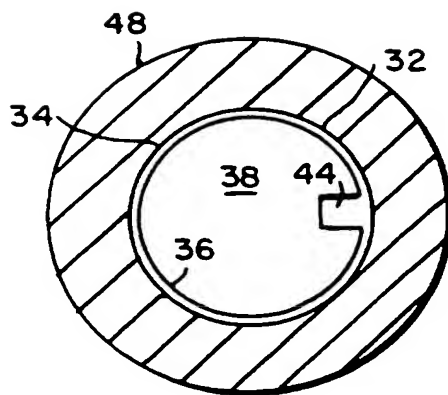
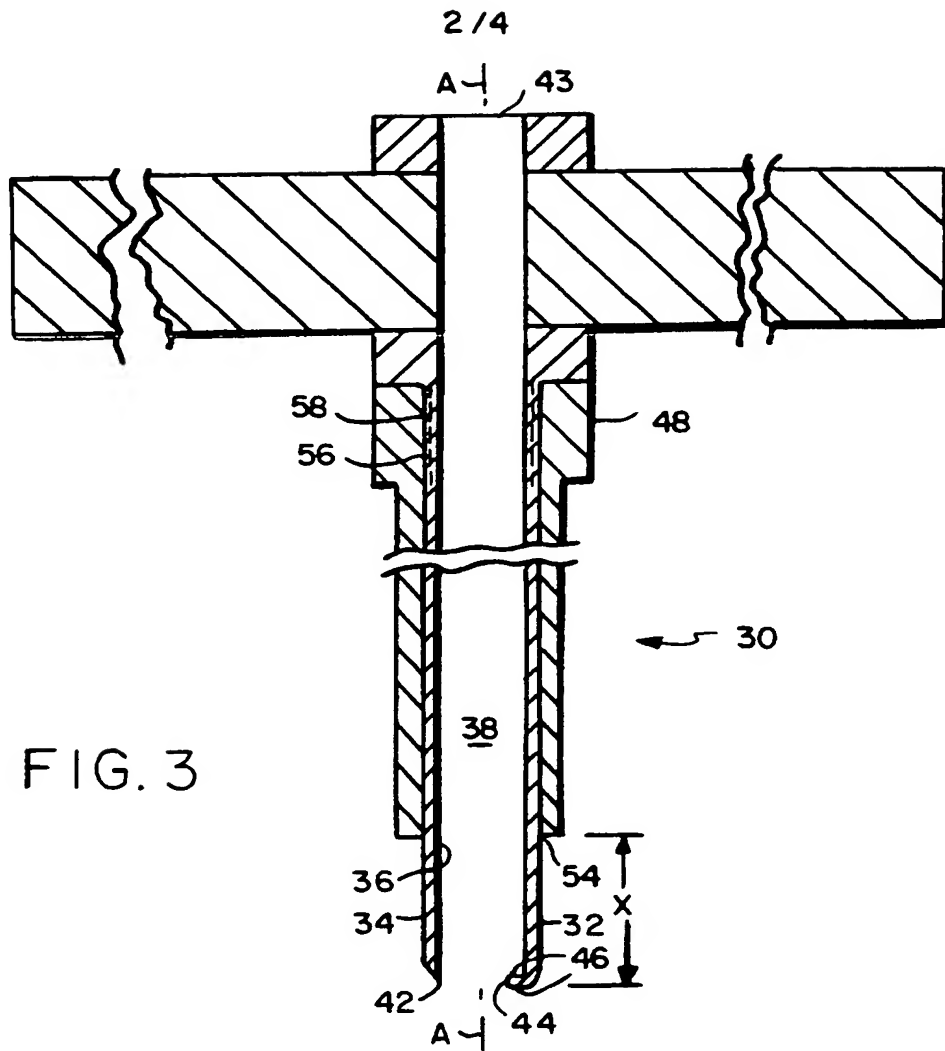


FIG. 2

SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)

3/4

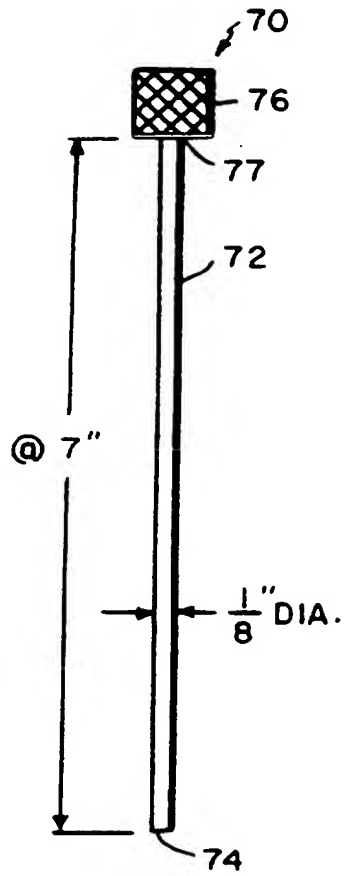


FIG. 5

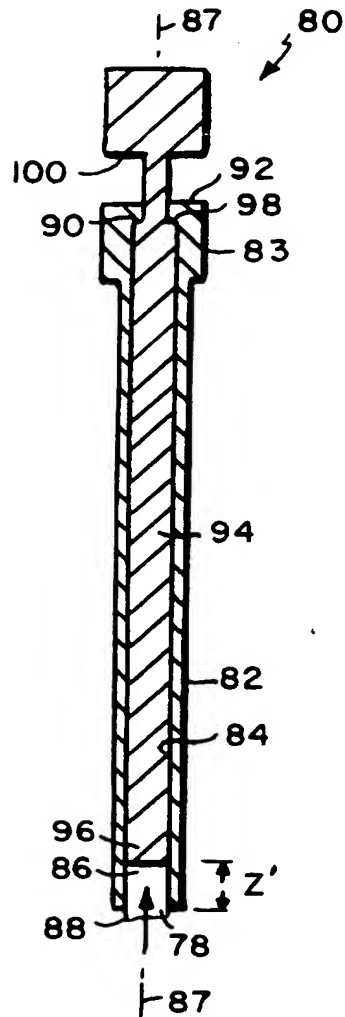


FIG. 6

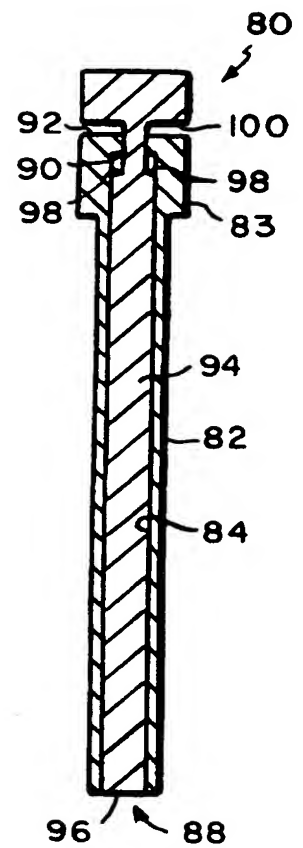


FIG. 7

SUBSTITUTE SHEET (RULE 26)

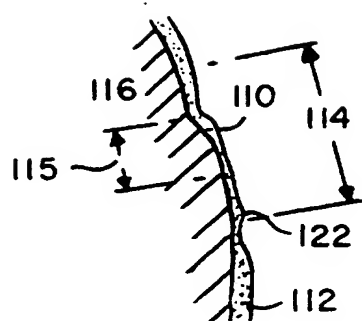


FIG. 8A

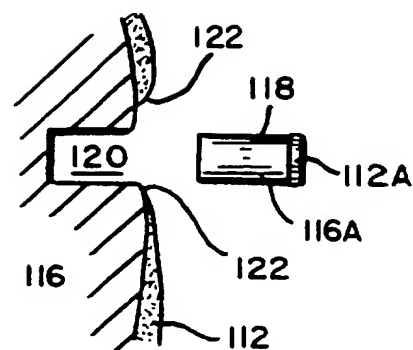


FIG. 8B

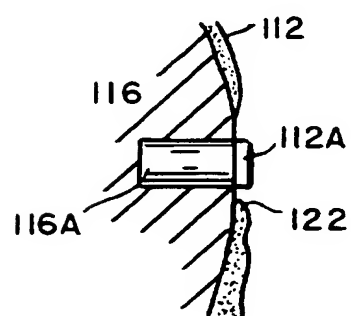


FIG. 8C

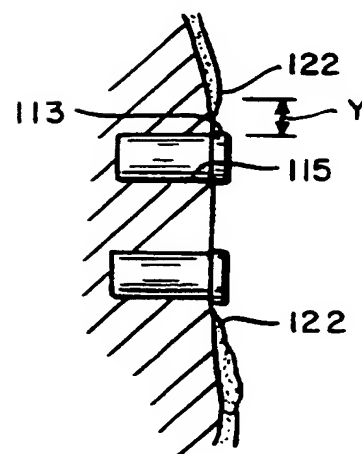


FIG. 8D

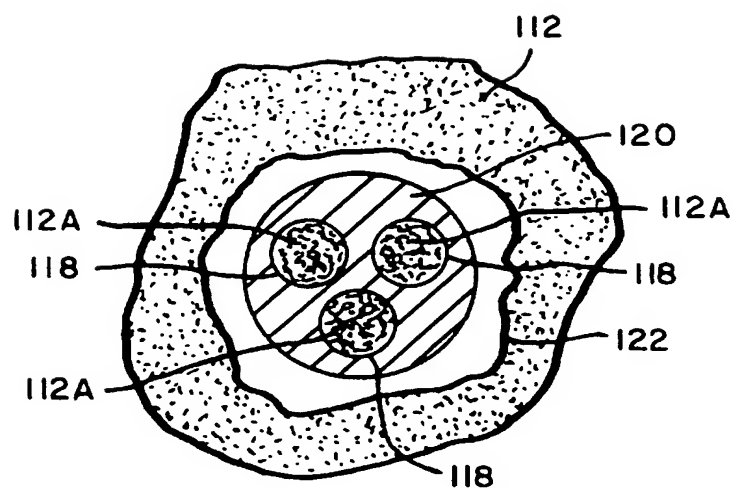


FIG. 9

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

Inter national Application No
PCT/US 96/01923

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B17/16 A61B17/32 A61F2/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	US,A,4 649 918 (PEGG) 17 March 1987 see the whole document	1-3,5,6, 8,10,29 17,20, 22,23,25
Y A	DE,U,93 12 792 (MAN CERAMICS) 7 October 1993 see the whole document	1-3,5,6, 8,10,29 19
Y A	US,A,3 848 601 (MA) 19 November 1974 see the whole document	14-16,28 1-3, 17-20,29
Y A	US,A,5 092 891 (KUMMER) 3 March 1992 see column 6, line 24 - column 7, line 6; figures 4,8,9	14-16,28 11,12, 17,26

	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

28 June 1996

Date of mailing of the international search report

03 07.96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Klein, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/01923

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE,U,86 01 068 (NATIONAL RESEARCH DEVELOPMENT CORPORATION) 3 April 1986 see the whole document ---	1,2
A	WO,A,83 02553 (MERCK PATENT) 4 August 1983 see abstract; figure 6 ---	1,8
A	US,A,4 559 936 (HILL) 24 December 1985 see the whole document ---	1,14,17, 28,29
A	US,A,4 059 115 (JUMASHEV) 22 November 1977 see abstract; figures 1,12-16 ---	2,15,18, 19
A	US,A,4 142 517 (STAVROPOULOS) 6 March 1979 see abstract; figures ---	2,15,19
A	US,A,4 873 991 (SKINNER) 17 October 1989 see column 4, line 28 - line 40; figures 3-11 ---	4-7, 21-24
A	US,A,4 293 962 (FUSON) 13 October 1981 see abstract; figures ---	14
A	WO,A,93 07819 (ELIAS) 29 April 1993 ---	
A	US,A,5 067 964 (RICHMOND) 26 November 1991 cited in the application ---	
A	EP,A,0 530 804 (SHAW) 10 March 1993 -----	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/01923

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 30-33
because they relate to subject matter not required to be searched by this Authority, namely:
PCT Rule 39.1(iv) Method for treatment of the human body by surgery
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 96/01923

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4649918	17-03-87	NONE	
DE-U-9312792	07-10-93	NONE	
US-A-3848601	19-11-74	NONE	
US-A-5092891	03-03-92	NONE	
DE-U-8601068	03-04-86	GB-A, B 2170127	30-07-86
WO-A-8302553	04-08-83	DE-A- 3202193	04-08-83
		EP-A, B 0099371	01-02-84
		JP-B- 3043900	04-07-91
		JP-T- 59500045	12-01-84
		US-A- 4895146	23-01-90
US-A-4559936	24-12-85	NONE	
US-A-4059115	22-11-77	NONE	
US-A-4142517	06-03-79	NONE	
US-A-4873991	17-10-89	US-A- 4903709	27-02-90
US-A-4293962	13-10-81	NONE	
WO-A-9307819	29-04-93	US-A- 5324300	28-06-94
		CA-A- 2099287	26-04-93
		EP-A- 0564630	13-10-93
US-A-5067964	26-11-91	EP-A- 0528080	24-02-93
EP-A-530804	10-03-93	US-A- 5270300	14-12-93
		AU-B- 657888	23-03-95
		AU-B- 2541192	05-04-93
		CA-A- 2116859	18-03-93
		JP-T- 7500741	26-01-95
		NO-A- 940764	29-04-94
		WO-A- 9304710	18-03-93
		ZA-A- 9206729	12-03-93